

CLONING AND REGULATION OF AN ENDOTHELIAL CELL
PROTEIN C/ACTIVATED PROTEIN C RECEPTOR

Abstract of the Invention

Human protein C and activated protein C were shown to bind to endothelium specifically, selectively and saturably ($K_d=30$ nM, 7000 sites per cell) in a Ca^{2+} dependent fashion. Expression cloning revealed a 1.3 kb CDNA that coded for a novel type I transmembrane glycoprotein capable of binding protein C. This protein appears to be a member of the CD1/MHC superfamily. Like thrombomodulin, the receptor involved in protein C activation, the endothelial cell protein C receptor (EPCR) function and message are both down regulated by exposure of endothelium to TNF. Identification of EPCR as a member of the CD1/MHC superfamily provides insights into the role of protein C in regulating the inflammatory response, and determination of methods for pharmaceutical use in manipulating the inflammatory response.